

# Drug induced gingival overgrowth

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### Abstract:

Gingival hyperplasia / hypertrophy is a rather common condition. This article reviews literature pertaining only to gingival overgrowth following drug ingestion. A wide range of causes have been attributed to gingival overgrowth. Drug induced overgrowth commonly occurs following medications prescribed for non dental causes. Pathogenesis of gingival overgrowth following ingestion of certain drugs is still unsure. Certain high risk co existant factors like presence of gingivitis has been implicated. Management of this condition should take into consideration the condition for which the offending drug has been prescribed. Physicians should be aware of drugs that could cause gingival overgrowth in order to identify and manage this problem.

### Introduction:

A large number of drugs have been implicated as cause for gingival hypertrophy / hyperplasia. Use of the term hypertrophy / hyperplasia is rather controversial. These terms do not accurately reflect the current understanding of the current histopathological scenario. Gingival enlargement in these patients is not due to increase in the number of periodontal cells but due to an increase in the extracellular volume <sup>1</sup>. This increase in the extracellular volume is caused by hyperplasia involving fibroblasts.

Gingival overgrowth was first described in dental literature of 1960's<sup>2</sup> when case reports started appearing about children who developed enlarged gingiva due to treatment of epilepsy using phenytoin. This condition was also described in children born of epileptic mothers who were being treated with sodium valproate. These children were branded to be suffering from fetal valproate syndrome <sup>3</sup>. Fetal valproate syndrome was first described by Di Liberti in 1984 <sup>4</sup>. These children also had neurodevelopmental problems. Associated congenital defects in this syndrome include Neural tube defects, congenital heart defects, orofacial clefts, and limb defects.

### Drugs involved in causing gingival enlargement:

Three types of drug categories <sup>6</sup> have been implicated as causative factors of gingival enlargement. They include:

1. Anti epileptic drugs – Phenytoin, Phenobarbitone, Valproic acid, Primidone, Vigabatrin and carbamazepine.
2. Calcium channel blockers – Nifedipine, Verapamil, Diltiazem and Amlodipin
3. Immunosuppressive drugs – Cyclosporine

Studies reveal that drug induced gingival overgrowth usually occurs within first three months of starting drug therapy with the offending drug. This usually begins as an enlargement involving Interdental papillae.

### Prevalance:

Review of literature shows a wide variation in prevalence rates <sup>7</sup>. A high figure of 50% has been quoted for the drug phenytoin, where as for cyclosporin it is 30% and for calcium channel blockers 10%. Recent studies have demonstrated the synergistic effect of cyclosporin with calcium channel blockers in causing gingival overgrowth <sup>8</sup>. Indian statistics are rather sketchy in this aspect. One study reports that 57% of epileptic children in the age group 8-13 on phenytoin developed gingival overgrowth within the first 3 months of starting the treatment<sup>9</sup>.

#### Etiology:

Etiology although enough pointers are there to point fingers at an offending drug, is still considered to be multifactorial. The relationship between the drug dosage, duration of therapy and sex predilection is still not clear. There is still a raging debate going on as to whether drug induced gingival hyperplasia could be caused by hyperplasia of gum epithelium or of subcutaneous connective tissue or both.

Certain predisposing risk factors have been indentified and documented. They include:

Poor oral hygiene: Presence of dental plaque can provide a reservoir for accumulation of drugs like phenytoin / cyclosporin<sup>8</sup>.

In patients who have undergone orthodontic procedures the presence of nickel could predispose to formation of gingival over growth

Susceptibility of some subpopulation of fibroblasts and keratinocytes to phenytoin, cyclosporin and other drugs which could cause gingival overgrowth

Number of langhans cells<sup>10</sup> present in the oral epithelium is another risk factor. More the number worse the risk. These drugs have a tendency to accumulate inside these cells causing prolonged effect on the gums.

Cytochrome P-450 gene polymorphism <sup>11</sup> can cause individual variations in drug metabolism predisposing to gingival overgrowth

In patients using calcium channel blockers gingival overgrowth could be caused by:

Defective collagenase activity

Blockage of aldosterone synthesis from adrenal cortex followed by feedback increase in the secretion of ACTH

Upregulation of keratinocytes growth factor

Upregulation of transforming growth factor alpha<sup>412</sup>

The tissue overgrowth is classically of dense collagen tissue and other connective tissue elements. Scattered inflammatory cells can also be seen. Classically gingival tissue adjacent to anterior teeth is more commonly affected than the posterior ones. Presence of bacterial plaque in the teeth is essential for gingival overgrowth to occur. Histology of overgrowth revealed hyperplasia of connctive tissue, epithelial acanthosis and elongated rete ridges.

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Picture showing gingival overgrowth



### Management:

Stopping / substituting the offending medicine. Gingival overgrowth reverts back to normal within 3 months.

Maintenance of strict oral hygiene

Regular mouth wash using chlorhexidine

Oral metronidazole for 21 days

Surgical removal of the gingival overgrowth (gingivectomy)

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